

AFRL-PR-WP-TM-2003-2013

**INTEGRATED mFLUME
RECONSTITUTION SYSTEM FOR
BIOLOGICAL AND MEDICAL
SUPPLIES**

**Integrated MEMS Delivery System for both
Liquid and Reconstituted Drugs**

Dorian Liepmann

**University of California at Berkeley
The Regents of the University of California, Berkeley
Sponsored Projects Office
336 Sproul Hall
Berkeley, CA 94720-5940**

NOVEMBER 2001

Final Report for 04 March 1997 – 04 February 2000



20030304 079

Approved for public release; distribution is unlimited.


**PROPULSION DIRECTORATE
AIR FORCE RESEARCH LABORATORY
AIR FORCE MATERIEL COMMAND
WRIGHT-PATTERSON AIR FORCE BASE, OH 45433-7251**

NOTICE


When Government drawings, specifications, or other data are used for any purpose other than in connection with a definitely Government-related procurement, the United States Government incurs no responsibility or any obligation whatsoever. The fact that the Government may have formulated or in any way supplied the said drawings, specifications, or other data, is not to be regarded by implication, or otherwise in any manner construed, as licensing the holder, or any other person or corporation; or as conveying any rights or permission to manufacturer, use, or sell any patented invention that may in any way be related thereto.

This report has been reviewed by the office of public affairs (ASC/PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

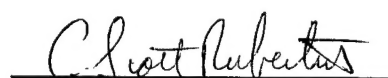
This technical report has been reviewed and is approved for publication.



KIRK L. YERKES, PhD
Project Engineer
Power Division



JOHN K. ERBACHER, PhD
Acting Chief, Energy Storage & Thermal Sciences Branch
Power Division



C. SCOTT RUBERTUS
Acting Deputy Chief
Power Division

Copies of this report should not be returned unless return is required by security considerations, contractual obligations, or notice on a specific document.

REPORT DOCUMENTATION PAGEForm Approved
OMB No. 0704-0188

The public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE (DD-MM-YY) November 2001		2. REPORT TYPE Final		3. DATES COVERED (From - To) 03/04/1997 – 02/04/2000	
4. TITLE AND SUBTITLE INTEGRATED mFLUME RECONSTITUTION SYSTEM FOR BIOLOGICAL AND MEDICAL SUPPLIES Integrated MEMS Delivery System for both Liquid and Reconstituted Drugs				5a. CONTRACT NUMBER N/A	
				5b. GRANT NUMBER F33615-97-1-2730	
				5c. PROGRAM ELEMENT NUMBER 69199F	
6. AUTHOR(S) Dorian Liepmann				5d. PROJECT NUMBER ARPP	
				5e. TASK NUMBER 97	
				5f. WORK UNIT NUMBER 05	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of California at Berkeley The Regents of the University of California, Berkeley Sponsored Projects Office 336 Sproul Hall Berkeley, CA 94720-5940				8. PERFORMING ORGANIZATION REPORT NUMBER FUND 25313-23795	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) Propulsion Directorate Air Force Research Laboratory Air Force Materiel Command Wright-Patterson Air Force Base, OH 45433-7251				10. SPONSORING/MONITORING AGENCY ACRONYM(S) AFRL/PRPS	
				11. SPONSORING/MONITORING AGENCY REPORT NUMBER(S) AFRL-PR-WP-TM-2003-2013	
12. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release; distribution is unlimited.					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT The overall goal of this project was to develop an integrated mFLUME system for the reconstitution, metering, and delivery of biological and medical supplies. This system would allow for the on-demand reconstitution of a wide range of medical supplies that have been stored in dry form for robustness, convenience, and shelf life. The MEMS system required the development and integration of micro-fluidic control components, including valves, pumps, mixing chambers, and fluid ejection ports, with dry material and solvent reservoirs and on-board electronic control systems. A fully integrated device for the reconstitution of a lyophilized drug was never created. However, under this contract, significant advances were made in the area of MEMS-based fluid control systems, including planar valves, mixers, pumps, and interconnects. In addition, integration of a working microFLUMES device into an injection-molded package was demonstrated under a contract extension. In addition, attention was brought to the MEMS community regarding micro-fluid mechanical processes, including the presence and effects of large momentum and scalar gradients.					
15. SUBJECT TERMS microelectromechanical device, MEMS, drug delivery, micro-fluidics					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT: SAR	18. NUMBER OF PAGES 10	19a. NAME OF RESPONSIBLE PERSON (Monitor) Kirk Yerkes 19b. TELEPHONE NUMBER (Include Area Code) (937) 255-5721
a. REPORT Unclassified	b. ABSTRACT Unclassified	c. THIS PAGE Unclassified			

Final Report

Integrated mFLUME Reconstitution System for Biological and Medical Supplies (Integrated MEMS Delivery System for both Liquid and Reconstituted Drugs)

Contract # F33615-97-1-2730

Dorian Liepmann
University of California at Berkeley

The overall goal of this project was to develop an integrated μ FLUME system for the reconstitution, metering, and delivering of biological and medical supplies. This system would allow for the on-demand reconstitution of a wide range of medical supplies that have been stored in dry form for robustness, convenience, and shelf life. The MEMS system required the development and integration of micro-fluidic control components, including valves, pumps, mixing chambers, and fluid ejection ports, with dry material and solvent reservoirs and on-board electronic control systems.

A fully integrated device for the reconstitution of a lyophilized drug was never created. However, under this contract significant advances were made in the area of MEMS-based fluid control systems including planar valves, mixers, pumps, and interconnects. In addition, integration of a working microFLUMES device into an injection molded package was demonstrated under a contract extension. In addition, attention was brought to the MEMS community regarding micro-fluid mechanical processes including the presence and effects of large momentum and scalar gradients. Specific developments are described below.

Micro-Fluidic Interconnects

As with integrated circuits, packaging for fluidic MEMS devices can be a major expense. Typically, connecting to the outside world has involved aligning and gluing tubes to holes etched in the device surface. This sort of manual alignment is both costly and difficult. Therefore, we developed integrated interconnects which connect microfluidic devices to each other and also to the macroscopic world.

Using our experience in the development of micro-needles, a new interconnection approach was developed to both connect μ FLUME devices as well as providing an easy approach for fluid supply. The micro-needles are fabricated at the same time as the MEMS fluid control components. They can then be used to pierce membranes such as a vitamin capsule or membrane covering the port for another device.

Planar Micro-Valves

The work at Berkeley focused on the development of integrable, planar components because of the high development and manufacturing costs predicted for multi-layer MEMS devices. Initially we used gas-liquid interfaces to generate and control fluid motion using thermal phase changes. However, this approach required too much power for portable devices and had unexpected and

undesirable effects specifically in valves. Because of these issues, we developed micro-valves that contain moving parts fabricated *in situ*. Our approach used prebonded Silicon On Insulator (SOI) wafers in conjunction with Deep REI etching. Using this approach we developed under this contract, the first controlled planar micro-valves as well as the first micro check-valves with moving components.

Micro-pumps

Two different micro-pumps were developed under the contract. The first extended our approach of using phase change to create a positive-displacement pump. Positive displacement approach is ideal for MEMS devices because they are characterized by high head pressure, although they generally have low flow rates. However, these characteristics work extremely well for most MEMS applications. The check-valves provided the missing component because of their unique viscous-driven actuation as well as their extremely high pressure drop in the closed position. These devices have been demonstrated to work for over 12 hours continuously.

The second micro-pumps provide faster flow rates and are completely reversible. They use marangoni flows generated by small temperature gradients across a thermal or other bubble. While these devices do not generate high head pressure, they can generate high flow rates. Our initial prototypes used thermal bubbles because of their controllability. This was found to require significant power because the device heats up. An additional advantage is their ease of fabrication; only heaters are needed, without the need for moving parts.

Micro-pumps and Mixer

The first truly integrated MEMS fluidic device, a controlled micromixer, was developed under this contract. This device is entirely self-contained and only requires inputs and outputs for fluids and power. To make this micro-mixer, two positive displacement micro-pumps provide time-dependent flows into a channel. Because of the efficiency of the check-valves, the pumps demonstrated significant improvements over previous pumps.

Device Integration in an Injection Molded assembly

Under a contract extension, the micro-mixer was integrated into a plastic, injection-molded housing. This project was performed to investigate techniques to create hybrid devices as well as improving our ability to create fluidic interconnects.

Wetting and Flow Studies

For the drug delivery system, a quantity of freeze-dried drug must be attached from which doses can be taken and injected into the body. The original idea was to have a reservoir filled with the drug, an external pressurized water source connected at one end, and a connection to a MEMS mixing and injection device on the other. Shortly before the first injection, the reservoir would be flooded with water, which would quickly become saturated. A microvalve in the MEMS device would allow for small quantities of saturated solution to be drawn off. As each dose was removed, pure water would enter the reconstitution chamber. If the output volume flow rate were small enough, the incoming pure water would become saturated before exiting. Therefore, the output from the drug reservoir would remain saturated for many doses.

Reservoir Filling and Sealing

Significant work has been done to develop ways to improve sealing and filling of MEMS devices. The approaches were reported at the Second PI Meeting. These approaches included the use of patterned photoresist to seal micro-fluidic systems and the use of small channels that will allow air to escape from dead end passages.

In addition, we have designed procedures to implement epoxy in a device with electrical circuits and sealed flow structure. A proposed solution to the problems observed during the preliminary trials calls for fabricating the epoxy flow structure over electrical circuits and capped with a flat surface that is coated with unexposed epoxy. The unexposed epoxy should conform to the slight difference in the feature thickness and will then be exposed to properly seal the flow structure.

Interconnects and Seals

With the demonstration of sealed epoxy channel, we extended the concept to design a process that would produce sealed channels, fluid access ports, thermal isolation to key components and access to electrical through a batch process that may be more commercially viable. As an added benefit, the channels are optically transparent from all sides and could be valuable in flow visualization.

Publications

Debar MJ and Liepmann D. (2002). "Fabrication and performance testing of a steady thermocapillary pump with no moving parts." Proceedings of the MEMS 2002 IEEE International Conference. Fifteenth IEEE International Conference on Micro Electro Mechanical Systems (Cat. No.02CH37266), Las Vegas, NV, USA, 109-112.

Liepmann, D., (2001) "Delivery, acquisition and control of fluids for BioMEMS applications," Proceedings of The 3rd Korean MEMS Conference, 13-14, April 2001, Seoul National University, Seoul Korea.

Zahn, J. D., Deshmukh, A. A., Pisano, A. P. and Liepmann, D. (2001). "Continuous on-chip micropumping through a microneedle". 14th IEEE International Conference on Micro Electro Mechanical Systems, Interlaken, Switzerland, 21-25 Jan. 2001, 503-6.

Liepmann, D., (2000). "Drug Delivery, Microfluidics, and MEMS." Proceedings of ICMMB-11: International Conference on Mechanics in Medicine and Biology, Maui, Hawaii, April 2-5, 2000.

Scalf, J., Liepmann, D. and Pisano, A. P. (2000). "Bulk-etched integrated mesoscopic fluidic interconnects for fluidic microdevices". The Electrochemical Society (World Meeting Number 004 0642), Phoenix, Arizona (USA), 22-27 October, 2000.

Papavasiliou, A. P., Liepmann, D. and Pisano, A. P. (2000). "Electrolysis-bubble actuated gate valve [for insulin injection application]". Solid-State Sensor and Actuator Workshop, Hilton Head Island, SC, 4-8 June, 48-51.

Kirshberg, J., Yerkes, K. L. and Liepmann, D. (2000). "Demonstration of a micro-CPL based on MEMS fabrication technologies". 35th Intersociety Energy Conversion Engineering Conference, Las Vegas, NV, USA, 24-28 July 2000, 1198-204 vol.2.

Desmukh, A. A., Liepmann, D. and Pisano, A. P. (2000). "Continuous micromixer with pulsatile micropumps". Solid-State Sensor and Actuator Workshop, Hilton Head Island, SC, USA, 4-8 June 2000, 73-6.

Papavasiliou, A.P., Liepmann, D., and Pisano, A.P., (1999) "Fabrication of a Free Floating Silicon Gate Valve," Proceedings of the ASME MEMS Division, 1999 IMECE, Vol.1 pp 435-440.

Evans, J. D. and Liepmann, D., (1999) "The Bubble Spring and Channel (BsaC) Valve: An Actuated, Bi-Stable Mechanical Valve for In-Plane Fluid Control," *Transducers '99, The 10th International Conference on Solid-State Sensors and Actuators*, Sendai, Japan, June 7 – 10, 1999.

Evans, J. D. and Liepmann, D., (1999) "The 'Spring Valve' Mechanical Check Valve for In-Plane Fluid Control," *Transducers '99, The 10th International Conference on Solid-State Sensors and Actuators*, Sendai, Japan, June 7 – 10, 1999.

Evans, J.D., Liepmann, D. and Pisano, A.P. (1997) "Planar Laminar Mixer", MEMS97 (The Tenth Annual International Workshop on Micro Electro Mechanical Systems), January 26-30, 1997, Nagoya, Japan, pp. 96-101. (IEEE Catalog Number 97CH36021).